61. (New) The composition of claim 41, further comprising an amount of the polynucleotide sufficient to elicit an anti-HMFG immunological response.

REMARKS

Status of the claims; request for rejoinder

Of originally submitted claims 1-58, claims 1-5, 20-37, 39-40, 42, 43, 46-56 are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions. By this amendment, claim 13 is cancelled and claims 6-12, 14-19, 38, 41, 44-45, and 57-58 are under examination. Support for the claim amendments is found in the specification at, inter alia, page 11, lines 24-35; page 32, lines 30-37; page 16, lines 17-22; page 17, lines 8-14.

Applicants request rejoinder of presently excluded method claims, to the extent that they incorporate all the limitations of the product claims.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Amendments to the specification

As requested by the Examiner, (a) the title has been amended to be clearly indicative of the invention to which the claims are directed; (b) the address of the ATCC on page 8, line 28 has been corrected; the blanks on page 1 (lines 6-8), page 8 (line 32) and page 46, (line 29) have been replaced with the appropriate serial numbers; and (c) the continuing data on the first line of the specification has been amended.

Applicants respectfully request that the Examiner remove objections to the specification.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 6-19, 38, 41, 44, 45, and 57-58 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite.

Claims 6-13, 16-19, 38, 41, 44-45, 57-58. Claims 6-13, 16-19, 38, 41, 44-45, 57-58 are allegedly indefinite for reciting "polypeptide having immunological activity of monoclonal anti-idiotype antibody 11D10". The Examiner states it is not clear what sort of immunologic activity is being claimed. As amended, claim 6 (and thus its dependents) recites "capable of eliciting an anti-HMFG immunological response in a mammal." Applicants call the Examiner's attention to the claims of U.S. Pat. No. 5,935,812 (the application for which the Examiner examined), which recite the same language. Applicants respectfully request withdrawal of this rejection.

Claims 6-13, 16-19, 38, 41, 44-45, 57-58. Claims 6-13, 16-19, 38, 41, 44-45, 57-58 are allegedly indefinite in the recitation of "11D10" because other laboratories or inventors may use the same laboratory designation to refer to different antibodies. Applicants appreciate the Examiner's suggestion and have amended claim 6 to recite the corresponding ATCC accession number, which the Examiner indicated would overcome this rejection. Applicants respectfully request withdrawal of this rejection.

Claims 9-12. Claims 9-12 are allegedly indefinite for reciting sequence "depicted within". These claims have been amended to recite "contained in". This phrase is found in U.S. Patent 5,935,821 (issued August 10, 1999), the application for which the Examiner examined. Applicants respectfully request withdrawal of this rejection.

Claim 13. Claim 13 is allegedly indefinite for reciting "complementarity defining region" rather than the commonly-used term "complementarity determining region." Applicants have cancelled claim 13, rendering this rejection moot. Applicants respectfully request withdrawal of this rejection.

Claims 14-15 and 57-58. Claims 14-15 and 57-58 are allegedly indefinite for reciting "said region capable of forming a stable duplex with . . . under conditions where the region does not form a stable hybrid with SEQ ID NO: 5 through 14."

First, the Examiner objected to use of the term "capable." Applicants believe that the phrase "capable of forming a stable duplex" would be clear to one skilled in the art to mean forming a stable duplex under appropriate hybridization conditions. However, in the interest of expediting prosecution, Applicants have amended the claims to recite "said region forming a stable duplex."

Second, the Examiner stated that it is not clear what conditions are being claimed. The claims have been amended to recite that the conditions are " hybridization conditions of 68°C and 0.15 M NaCl and 15 mM citrate buffer (1 X SSC)."

Third, the Examiner requested clarification as to which 15 contiguous nucleotides of which sequences are forming the stable duplex. As amended, claims 14 and 15 contain language further defining the 15 contiguous nucleotides forming the stable duplex and contained in SEQ. ID NO:1 or SEQ. ID NO:3, respectively.

Fourth, the Examiner objected to the fact that the terms "stable duplex" and stable hybrid" are both used in claims 14 and 15 interchangeably and nonuniformly. Applicants have amended claims 14 and 15 to use only the term "duplex" and have deleted the term "hybrid" from these claims.

Fifth, the Examiner objected to the language "SEQ. ID NO:5 through 14." This phrase has been deleted from the claims, rendering this rejection moot.

Sixth, the Examiner objected to the claim language "the region does not form a stable hybrid with [a sequence]." Claims 14 and 15 have been amended such that this language has been deleted, rendering this rejection moot.

Applicants respectfully request withdrawal of this rejection.

Claim 38. Claim 38 is allegedly indefinite for reciting "a pharmaceutical composition." Applicants appreciate the Examiner's suggestion and have deleted the term "pharmaceutical"

from claim 38, thereby obviating the Examiner's rejection. Applicants respectfully request withdrawal of this rejection.

Claims 38 and 41. The Examiner stated that claims 38 and 41 are indefinite for reciting "effective amount". Applicants have amended claims 38 and 41 to delete this phrase in accordance with the Examiner's suggestion (Office Action, page 11). The claims as amended recite that the compositions of the claim comprise a polynucleotide and a pharmaceutically acceptable excipient. Applicants respectfully request withdrawal of this rejection.

In view of the above, Applicants respectfully request that all rejections under § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 6-19, 38, 41, 44, 45, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as allegedly non-enabled for vaccines, and polynucleotides encoding portions of 11D10.

Claims 6-19, 38, 41, 44-45, and 57-58. Although these claims were indicated as rejected under 35 U.S.C. §112, first paragraph, the Examiner only refers to rejections under 35 U.S.C, § 112, second paragraph. Those rejections have been addressed above. In accordance with the Examiner's suggestion, these claims have been amended to recite the particular type of immunological activity (namely, eliciting an anti-HMFG immunological response in a mammal). The claims have also been amended to recite that the polypeptide encoded by the claimed polynucleotide comprises three CDRs from the light chain or the heavy chain of 11D10. Given the Examiner's position with respect to previously reported polypeptides that contain only 5 or more amino acids from 11D10, this language should be satisfactory. The Examiner points to a paper which discloses a polypeptide that contains only 5 amino acids from the variable region of 11D10 (Mo et al.) and states that "[o]ne skilled in the art would reasonably conclude that immunization with Mo et al.'s polypeptide would result in antibodies which also bind to the 11D10 antibody." Office Action, page 13. The Examiner repeats the same statement for seven other references which allegedly disclosed polypeptides which contain 5 or more amino acids

from the variable region of 11D10. If the Examiner believes that a polypeptide that contains only 5 amino acids in the variable region of 11D10 would elicit anti-11D10 antibodies, then the claims as submitted are enabled.

The Examiner also discusses the requirements for formation of an antigen-binding site.[1] As is well known in the art, the requirements for immunostimulation by a polypeptide are less stringent than those for binding of antigen to antibody, and peptides as small as 5 amino acids in length can be immunogenic. As noted above, the Examiner herself stated that a polypeptide that contained only 5 amino acids from a variable region of 11D10 would be expected to result in antibodies which also bind to the 11D10 antibody.

The Examiner's attention is also directed to U.S. Patent No. 5,935,821, the application for which was examined by the Examiner. Based on virtually identical facts, the Office issued claims which recite that the polypeptide encoded by the claimed polynucleotide comprises three light chain CDRs or three heavy chain CDRs from the anti-idiotype antibody.

Applicants respectfully request that this rejection be withdrawn.

Claim 14-15 and 57-58. Claims 14-15 and 57-58 were rejected for failing to teach hybridization conditions that would enable one skilled in the art to make and use the claimed polynucleotides without undue experimentation. Applicants respectfully point out that page 32 of the specification teaches appropriate hybridization conditions that would enable one skilled in the art to make and use this invention. Specifically, the last paragraph of page 32 teaches appropriate temperature, salt and formamide concentration, and wash conditions that would enable one skilled in the art to vary the stringency of the hybridization medium without undue experimentation. One skilled in the art would be able to use the information disclosed on page 32 of the specification and without undue experimentation, would be able to develop hybridization conditions that would permit formation of the stable duplex described in claims 14-

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[1] Applicants note that some of the text of this discussion did not pertain to the claims, and, to that extent, will not be addressed in this response. For example, the Examiner refers to "fusion proteins as defined by the claims" and "functional humanized antibody".

15 and 57-58. However, in the interest of expediting prosecution, and in accordance with the Examiner's suggestion, the claims have been amended to recite particular hybridization conditions. Applicants respectfully request withdrawal of this rejection.

Claim 38. The Examiner states that the phrase "effective amount" is indefinite when the claims fail to state the function which is to be achieved. In accordance with the Examiner's suggestion, Applicants have amended these claims to delete the phrase "effective amount". Applicants respectfully request withdrawal of this rejection.

Claims 38, 41, 44 and 45. Without acquiescing or agreeing with the Examiner's statements regarding vaccines, Applicants followed the Examiner's suggestion and have deleted the term "vaccine" in claims 41, 44, and 45 and have amended the claims to recite "immunogenic composition" instead, thereby obviating the Examiner's rejection. With respect to claim 38, Applicants have followed the Examiner's suggestion and have deleted the term "pharmaceutical". Applicants respectfully request withdrawal of this rejection.

In view of the above, Applicants respectfully request withdrawal of all rejections under § 112, first paragraph.

Rejections under 35 U.S.C. § 102

102(b) rejections

Mo et al. Claims 6, 8, 10, 12, 13, 15-17, 19, 38, 41, 44, and 58 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Mo et al. According to the Examiner, Mo et al. disclose polynucleotides that encode a polypeptide including five amino acids from the 11D10 heavy chain CDR 1 (SYNMH). Claim 6 (and thus its dependents) has been amended to recite that the polynucleotide encodes a polypeptide comprising three CDRs from the light variable region or three CDRs from the heavy variable region of 11D10, which is not encompassed by the cited sequence. Applicants respectfully request that this rejection be withdrawn.

Liu et al. and De Waele et al. Claims 6, 8, 10, 12, 13, 15-17, 19, 38, 41, 44, and 58 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by either Liu et al. or De Waele et al.

According to the Examiner, Liu et al. teach polynucleotides that encode a polypeptide comprising at least five amino acids of the 11D10 heavy chain variable region, including five amino acids from the 11D10 heavy chain CDR2. De Waele et al. allegedly teach polynucleotides that encode a polypeptide comprising at least five amino acids of the 11D10 variable region. Claim 6 (and thus its dependents) has been amended to recite that the polynucleotide encodes a polypeptide comprising three CDRs from the light variable region or three CDRs from the heavy variable region of 11D10, which is not encompassed by the cited sequence. Applicants respectfully request that this rejection be withdrawn.

Shlomchik et al., Kavaler et al., Seidman et al., and Darsley et al. Claims 6, 7, 9, 11, 14, 16, 17, 19, 41, 44, and 57 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by any of Shlomchik et al, Kavaler et al., Seidman et al., or Darsley et al. Each of these references allegedly teach polynucleotides that encode a polypeptide comprising at least five amino acids of the 11D10 light chain variable region. Claim 6 has been amended to recite that the polynucleotide encodes a polypeptide comprising three CDRs from the light variable region or three CDRs from the heavy variable region of 11D10, which is not encompassed by the cited sequence. Applicants respectfully request that this rejection be withdrawn.

Chatterjee et al. and Chakraborty et al. Claims 6-17, 19, 38, 41, 44, 57 and 58 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by any of Chatterjee et al. (Antigen and Antibody Molecular Engineering 1994); Chatterjee et al. (Cancer Immunol Immunother 1994), Chakraborty et al. (Proc Am Assoc Cancer Res 1994), or Chakraborty et al. (J Immunotherapy Vol 18). The Examiner states that although the DNA sequence encoding the 11D10 antibody was not disclosed in any of these cited references, the DNA is considered an inherent property of the hybridoma expressing the 11D10 antibody.

Applicants traverse this rejection. Disclosure of 11D10 a hybridoma producing 11D10, without more, would not enable one skilled in the art to deduce the polynucleotide sequence encoding the heavy or light chain variable regions of 11D10. During prosecution of related application U.S. Ser. No. 08/766,350, Applicants explained why prior publications referencing

antibody 11D10, but not disclosing the sequence of 11D10, were insufficient to place the claimed invention into the hands of the public, based on the mechanism of antibody formation. Applicants also filed declarations by Malaya (Bhattacharya-) Chatterjee, Kenneth Foon, and Sunil Chatterjee stating that, to the best of their knowledge and belief, neither the 11D10 antibody nor the 11D10 producing hybridoma cell line were made accessible to the public prior to the filing of the application. Copies of these declarations accompanies this response.

By the same line of reasoning as presented in prosecution of related application U.S. Ser. No. 08/766,350, the non-disclosure and unavailability of the 11D10 antibody, the hybridoma cell line, and the sequence means that the claimed invention was not in the hands of the public. Accordingly, Applicants respectfully request withdrawal of this rejection.

102(e) rejections

Gourlie et al. Claims 6, 8, 10, 12, 13, 15-17, 19, 38, 41, 44, and 58 are rejected under 35 U.S.C. 102(e) as allegedly anticipated by Gourlie et al. According to the Examiner, Gourlie et al. teach the sequence VRSGA. However, the Examiner is incorrect in stating that this 5-mer sequence consists of CDR1 of SEQ ID NO:4 (heavy chain variable region). As Figures 2 and 3B make clear, VRSGA is a portion of the first framework region (fr-1), which is depicted as amino acids 1-30.

Claim 6 (and thus its dependents) has been amended to recite that the polynucleotide encodes a polypeptide comprising three CDRs from the light variable region or three CDRs from the heavy variable region of 11D10, which is not encompassed by the cited sequence. Applicants respectfully request that this rejection be withdrawn.

Bendig et al. Claims 6, 7, 9, 11, 13, 14, 16, 17, 19, 38, 41, 44, and 57 are rejected under 35 U.S.C. 102(e) as allegedly anticipated by Bendig et al. According to the Examiner, Bendig et al. teach an antibody comprising the sequence MTQSPSSLSAS. The Examiner is incorrect in stating that this sequence "exactly matches the amino acid residues 24-34 of SEQ. ID NO:2, CDR 1 of the light chain of 11D10." As Figures 1 and 3A make clear, this sequence is part of the first framework region (fr-2), which is depicted as amino acids 1-23.

Claim 6 (and its dependents) has been amended to recite that the polynucleotide encodes a polypeptide comprising three CDRs from the light or heavy variable region(s) of 11D10, which is not encompassed by the cited sequence. Applicants respectfully request that this rejection be withdrawn.

102(f) rejection

Claims 6-17, 19, 38, 41, 44, 57, and 58 are rejected under 35 U.S.C. 102(f) by any of Chatterjee et al. (Antigen and Antibody Molecular Engineering 1994), Chatterjee et al. (Cancer Immunol Immunother 1994), Chakraborty et al. (Proc Am Assoc Cancer Res 1994), or Chakraborty et al. (J Immunotherapy Vol 18).

Accompanying this response is a copy of the declaration of Dr. Malaya Chatterjee, which addresses this issue. This declaration was submitted during prosecution of related application U.S. Serial No. 08/766,350. Dr. Chatterjee's declaration states that she chose the protocols and criteria to be followed for developing and selecting the 11D10 antibody; that she instructed Drs. Mrozek and Mukerjee to follow these protocols; that they reported the results of their experiments to her; and that she chose 11D10 as the most desirable antibody. Dr. Chatterjee's declaration also states that Drs. Mrozek, Mukerjee and Chakraborty did not make any independent contributions to generating 11D10 or the 11D10 producing cell line. They were all working under Dr. Chatterjee's direct supervision.

Applicants respectfully request withdrawal of this rejection.

Provisional Statutory Double Patenting Rejection

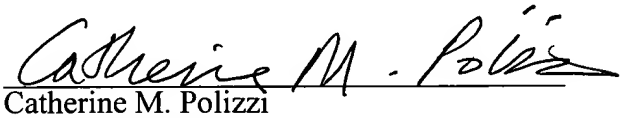
Claim 19 is provisionally rejected under the judicially created doctrine of double patenting over claim 3 of copending U.S. Serial Nos. 08/766,350 and 08/766,350, which recite a hybridoma expressing 11D10 monoclonal antibody. Claim 19 has been amended to recite "wherein the polynucleotide is a recombinant polynucleotide". The Examiner's attention is drawn to the claims of U.S. Patent 5,935,821, the application for which was examined by the Examiner. Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants believe they have addressed all issues raised by the Office and that the claims are in condition for allowance, which is respectfully requested. If the Examiner wishes to discuss this application or provide comments, she is invited to telephone Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 304142000322. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: November 17, 1999 By: 

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